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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/693,383

10/24/2003

Shalaby W. Shalaby

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03/06/2008

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EXAMINER

SILVERMAN, ERIC E

ART UNIT

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1618

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/693,383	Applicant(s) SHALABY ET AL.	
	Examiner Eric E. Silverman, PhD	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/28/2008 has been entered.

Pursuant to amendment, claims 1 – 15 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4 - 7, 9, and 11 – 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Instant claim 1 recites that the functional polymer is a carboxyl bearing copolyester. The original disclosure does not provide sufficient support for the entire genus of carboxyl bearing copolyester, rather, the original disclosure only supports a

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few specific species of carboxyl bearing copolyester, such as those mentioned in original claim 3 and paragraph [0016] of the published Application. The disclosed carboxyl bearing copolyesters are all members of a closely related group of nonionic biodegradable, bioabsorbable materials. These closely related materials are not representative of the entire genus of carboxyl bearing copolyesters, which may be non-biodegradable, non-bioabsorbable, ionic, or some combination thereof; the disclosed group is therefore insufficient to support the entire genus now claimed.

The remaining claims are rejected for depending on claim 1 without curing this issue, thereby incorporating the new matter into their own limitations.

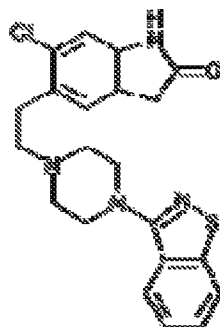
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 – 8, and 10 – 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,232,304 to Kim in view of US 5,916,833 to Shalaby et al.

Kim teaches that ziprasidone is advantageously made into ionic conjugates with cyclodextrin (abstract, examples). The solubility of ziprasidone is increased upon forming the conjugate (see table 1, first entry – HPBCD and SBECD are types of cyclodextrins). Ziprasidone reads on the pharmaceutical compounds of claims 4, 5, 12 and 13, and notably contains an amine group (the chemical structure of ziprasidone is well known in the art, and appears below).



Ziprasidone

What is lacking are the copolyester polymers of the instant claims, the grafted cyclodextrin-copolyester polymer of claim 3, the use of an organic solvent of claim 11.

Shalaby teaches cyclodextrins having polymers such as polylactide, polyglycolide, and polycaprolactone grafted onto them (table II, examples 1 and 2). Shalaby calls these materials ACDs, and they read on the polymers of instant claims. Shalaby suggests that these polymers are useful for forming conjugates with drugs having ionizable amine groups (col. 1 - col. 3). The use of the cyclodextrin grafted with the polymers of Shalaby is especially advantageous because it allows the drug to be released in a controlled manner (example 5 and table V). The method of making the drug-polymer conjugate uses acetone, an organic solvent, to dissolve the drug and ACD (example 3), reading on the organic solvent of claim 11.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to use the ACDs of Shalaby and the organic solvent acetone instead of the "regular" cyclodextrins of Kim. The motivation comes from Shalaby's teaching that controlled release of active agent can be effected by using ACDs, which the artisan would recognize as an improvement on Kim, who teaches only improved

solubility. The artisan would be merely following the artisans' suggestion in using acetone because that solvent is suggested for use with the ACDs.

Obviousness also stems from Shalaby's statement that the ACDs are useful with drugs containing an ionizable amine; Ziprasidone has at least two ionizable amines (the tertiary amines in the 1 and 6 position of the six-membered ring are ionizable), and as such, the artisan would immediately recognize that Ziprasidone meets Shalaby's requirements for drugs useful with ACDs. The fact that ziprasidone has been previously used with cyclodextrins to great effect (as in Kim) would have made it a particularly appealing drug to use with ACDs, and also goes towards the expectation of success. Because ziprasidone was used successfully with "regular" cyclodextrins in Kim, the artisan would expect it to work with the modified cyclodextrin ACDs of Shalaby.

Obviousness further stems from the fact that the claimed invention is no more than picking art-known materials and combining them in manner to obtain predictable, art-expected results. Shalaby teaches the copoly lactide-cyclodextrin graft of instant claims. Shalaby teaches that this graft is useful to conjugate with drugs having ionizable amines. Ziprosadone is a drug having at least one ionizable amine. Kim shows that ziprosadone is known in the art to be useful when conjugated to a cyclodextrin. The purpose of the cyclodextrin is to increase water solubility, and the purpose of the copolyester is to affect sustained release. Instantly claimed invention has no material properties other than those which the art recognizes and expects to stem from this combination, and therefore is obvious over the art.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,232,304 to Kim in view of US 5,916,833 to Shalaby et al., as applied to claims 1 – 8 and 10 – 15, above, and further in view of US 3,418,329 to Roberts et al.

What is lacking from Kim and Shalaby is the teaching of a vegetable oil.

Roberts teaches that in the art of carriers, vegetable oil and water are both useful for the same purpose, namely, as carriers for drug composition, specifically those to be used for parenteral delivery (col. 3, lines 25 – 26).

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to use vegetable oil as the carrier in Kim and Shalaby. Obviousness stems from the fact that such a use is merely the combination of art suggested drug-polymer conjugates with an art recognized carrier, wherein each component carries out its predictable recognized function.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

With respect to the rejection under 35 U.S.C. 112, 1st paragraph, the claim amendments have necessitated new rejections under that statute, for reasons unrelated to Applicants arguments.

With respect to the arguments against the rejection under 35 U.S.C. 103(a) under Kim and Shalaby, it is noted that the claims under rejection are different from those pending at the time of arguments, and the grounds for rejection are somewhat

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different as well. To the extent that the arguments in the most recent response are still relevant, they addressed here.

Applicant first argues there is no motivation to combine Kim and Shalaby because the problem solved by Kim is different from that solved by Shalaby. This argument is not well understood. To the extent that Applicant is trying to argue that the references are not analogous art, it is noted that both references discuss advantages gained from making ionic conjugates of drugs with cyclodextrins, which is also subject matter recited in the instant claims. Applicants then aver that the Office has not provided any reason why the references are combined to reach the claimed invention. In response, the rejection above lists no less than three reasons why Kim and Shalaby render the claims obvious. Briefly stated, the reasons are (1) Shalaby motivates the use of drugs with ACDs, and Kim's teaching that ziprosadone is effective when conjugated with "regular" cyclodextrins shows that success can be expected, (2) the use of ziprosadone, a drug with an ionizable amine, is no more than using a drug having the properties called for in Shalaby (Shalaby calls for drugs with ionizable amines) in the manner prescribed in Shalaby, and (3) the claimed invention is no more than the use of an art-known drug (ziprosadone) with an art-known agent that conjugates to drugs (ACDs), when the drug is already known to conjugate successfully to similar materials, where the results stemming from the combination are merely those predictable results that the art expects.

Applicants contention that it “would be error and is beyond common sense” to combine Kim and Shalaby is a mere allegation of patentability, based neither in facts of record nor in technical reasoning, and is not persuasive.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is (571)272-5549. The examiner can normally be reached on Monday to Thursday 7:00 am to 5:00 pm and Friday 7:00 am to noon.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Michael Hartley can be reached on 571 272 0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric E Silverman, PhD/

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